REMARKS

First, appreciation is expressed to the examiner for the courteous and helpful interview of May 22, 2009. It is believed that the foregoing amendments and the following remarks place this case into condition for allowance. Furthermore, appreciation is expressed for the examiner's very careful review of the claims and specification as indicated in the extensive Office Action.

General Background

As stated in the specification, it is known that increased levels of adrenomedullin (ADM), above those found in healthy persons, have been correlated in the prior art with various disease states. See, e.g., the first full paragraph on page 4 which lists some of these states known from the prior art, including congestive heart failure, kidney diseases, hypertensive disorders, diabetes mellitus and sepsis. See also the enclosed Kitamura and Ehlenz references. Thus, the invention does not involve the discovery that ADM is correlatable with disease states, insofar as such correlations have been known in the prior art.

A basic aspect of this invention is the discovery that a particular mid-regional partial peptide of proadrenomedullin (as recited in the claims) is present in biological fluids and provides a valuable indirect measure of ADM in such biological fluids. Thus, its measurement can serve the same function as measurement of ADM directly with respect to disease status. Measurement of the newly discovered partial peptide was heretofore not known as a basis on which ADM levels could be determined or disease status addressed. This is important because, as discussed in the specification

on pages 7 and 8, direct measurement of ADM in a biological fluid is beset by a variety of problems.

During the interview, the examiner suggested that the claims be reworded to recite determination of the mid-regional partial peptide. This suggestion has been adopted. See, e.g., page 14 of the specification. However, indirect determination of ADM is recited in claim 33. Support for the "indirect" nature of the adrenomedullin (ADM) determination is replete in the specification. Note in particular page 8, lines 22-25, page 8, line 31-page 9, line 4, page 14, lines 16-25, page 29, lines 10-16, etc.

Support for the "diagnosis, prognosis or therapy-accompanying monitoring" language, mentioned by the examiner, is at page 2, lines 1-4. This language clarifies the claims for the examiner's purpose but the claims require only the recited step of measuring. "Specific binding partner" is supported by the passage at page 12, lines 12-16, in context, and in view of conventional knowledge as of the priority date. The change to page 6 corrects a typographical error whose existence is clear from the explanation given on pages 13-16 of the response of September 29, 2008.

The following, for the sake of clarity, follows the order of the Office Action. Any items not specifically discussed below have been rendered moot by the foregoing amendments.

With respect to the restriction requirement mentioned on page 2 of the Office Action, Applicants request that the examiner reconsider the withdrawal of claims 13, 14 and 18. Because this application is based on a new method for measuring in a patient sample a heretofore unknown peptide correlated with ADM, no further searching is necessary for claims reciting a particular disease state of interest. Thus,

no burden is involved in maintaining all of the claims irrespective of the particular disease state recited. Patentability of the general determination step will necessarily render patentable employment of such step with respect to diagnosis or prognosis or therapy-accompanying monitoring of any disease.

The incorporation by reference issue discussed in paragraphs 13 through 16 is moot. Whereas various disclosures in the discussed WO 00/22439 and/or US 2004/0180396 may be of interest regarding support for the language of claims such as claims 20, 21, etc., these disclosures are not necessary to establish a written description of these claims. Rather, the specification disclosure at, e.g., page 10, lines 27-33 and page 7, lines 19-23, make clear that radioimmunoassays "are in principle not very suitable for delivering valuable knowledge on this question . . . do not appear very promising for the development aim of providing a valid assay for routine determinations." This disclosure indicates that, whereas RIAs could be used, they are not preferred. Both points independently support claims containing the negative limitation that a radioimmunoassay is not used. That the cited passages, especially that on page 10, provide support for the negative limitation is clear under the principles enunciated in MPEP 2173.05(i), which the examiner cites in the paragraph bridging pages 11 and 12 of the Office Action.

As discussed in the interview, the matter raised in items and 29 and 30 has been rendered moot by removal from the claims of the language to which the examiner objects. Thus, the specificity of the antibodies is now recited in terms of the partial peptide target without further characterization, as is conventional.

In paragraph 31 of the Office Action, the examiner raises linguistic problems concerning claim 9. The language above is based on the original version of claim 9 and is believed to eliminate the issue.

The questioned language from claim 23 (paragraph 32 of the Office Action) has now been replaced with language taken from page 6, lines 26-27. This renders moot the examiner's comments regarding a range with no upper limit.

With respect to paragraphs 33, 34 and 36 of the Office Action, the claims no longer refer to adrenomedullin "release." Rather, the claims are framed in terms of peptide determinations, as recited, e.g., on page 7, lines 7-19. Note also, for example, the first paragraph of the specification and its title, which are framed in terms of "determinations." See also the paragraph bridging pages 8 and 9, page 18, lines 13-18, among others.

As for the examiner's comment that there is no disclosure of the genus of diseases associated with increased ADM, the examiner is referred, in particular, to a partial listing of such diseases given on page 4 of the specification which, as mentioned, is taken from the prior art. See also the mentioned Kitamura and Ehlenz references, enclosed. When members of a genus are known in the prior art, the genus has a written description in a specification, even without explicit mention of those members. *Capon v. Eshhar, 418 F.3d 1349 (Fed. Cir. 2005).* The other questioned language regarding description of the human undergoing the assay has been removed.

The matter of paragraph 35 (claim 32) of the Office Action has been addressed by deleting the questioned language and instead basing the negative limitation on the discussion at page 6 of the specification, particularly lines 16-18. See also the

explanation given at pages 13-16 of the last response, especially with respect to the numbering (66-113) of the peptide.

The foregoing amendments are made to expedite allowance and render issues moot. No agreement with comments made in the Office Action is to be implied.

With respect to the enablement rejection of claims 27-29, it is believed that the foregoing claim language changes render this moot. No agreement with any aspect of the examiner's allegations is to be implied.

Moreover, as noted above, increased amounts of ADM have been correlated in the prior art with a number of diseases. This aspect and how to conduct such correlations are known. There is no enablement issue in this regard. Similarly, diseases correlated with increased ADM levels "other than sepsis" are clearly known in view of the foregoing discussion based, e.g., on page 4 of the specification and the attached references. In no way does the current or previous claim language imply that "any" disease (other than sepsis) was encompassed. It is only those diseases which correlate with increased ADM levels which are encompassed. As for the aspects of the claims which include prognosis or monitoring (now literally recited in the claims for further clarity), these aspects of the use of ADM values raise no enablement issues since these are conventionally performed irrespective of how the ADM levels are measured. It is the prior art knowledge concerning the known correlation of ADM with the diseases and their diagnosis, prognosis or monitoring which is relevant in this regard and not the fact that the mid-regional partial peptide is an inventive measurement basis.

Because the priority document has the same disclosure as the specification of this application, it is clear that it supports the claims for the same reasons that the current specification supports the claims. Consequently, the German priority is to be accorded to all claims of this application, whereupon all prior art rejections must be withdrawn since all are based on Bougueleret et al. as the primary or sole reference.

The examiner's double patenting rejections are all based on co-pending applications having U.S. filing dates much later than the U.S. filing date of this application. Under such circumstances, when the application on which the double patenting rejection is based is not allowed and the claims of the current application are allowed, then the double patenting rejection must be withdrawn. (MPEP § 804(I)(B)(1). Thus, as soon as the examiner allows the claims in view of this response, the cited MPEP passage will be controlling and all double patenting rejections must be withdrawn, except for U.S. Serial No. 11/997,250, which has now been issued as USP 7,547,553. A terminal disclaimer with respect to the latter is enclosed.

The change to the y-axis of the figures corrects obvious typographical errors. See, e.g., page 9, line 32 – page 10, line 21.

Respectfully submitted,

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Attorney Docket No.: VOSS-0043
Date: October 7, 2009
AJZ/tls